REMARKS

The Official Action dated October 19, 2011 has been carefully considered. Additionally, the telephone interview which the Examiner and his supervisor courteously afforded the undersigned on January 23, 2012 is acknowledged and appreciated. As discussed during the interview, it is believed the present claims are patentably distinguishable over the cited combinations of prior art and the present application is in condition for allowance. Reconsideration is respectfully requested.

According to claim 12, the system for determining microcirculation of a living tissue according to the present invention comprises (i) a white light source and a filter capable of illuminating a tissue surface with polarized light, (ii) a polarizing filter adapted to collect backscattered light subjected to multiple scattering events in the tissue; (iii) a photosensitive array capable of detecting the backscattered and polarized light and converting the detected light to a collected information of digital values; and (iv) a computing device adapted to receive said collected information, adapted to separate the collected information into data matrixes representing red, blue and green colors, respectively, and adapted to employ an algorithm using the data matrixes to generate an output data matrix representing the red blood cell concentration of the microcirculation.

As recited in claim 12, the system of the invention is adapted to collect backscattered light which has been subjected to multiple scattering events in the tissue. In conventional devices, such multiple scattering undesirably causes distortion in an image produced from the backscattered light. However, such distortion from multiple scattering can be significantly reduced in the presently claimed system as the computing device is adapted to separate the

collected information into data matrixes representing red, blue and green colors, respectively, and is adapted to employ an algorithm using the data matrixes to generate an output data matrix representing the red blood cell concentration of the microcirculation. Importantly, the digital values are separated into the red, blue and green data matrixes which are then used to generate the output data matrix and the values of the output data matrix relate linearly to the red blood cell concentration at each pixel.

The ability of the computing device to use the red, blue and green matrixes in an algorithm to form the output data matrix representing the red blood cell concentration of the microcirculation avoids or significantly reduces distortion problems from multiple scattering in tissue and adverse effects from fluctuating light intensity from an illuminating device. The algorithm which is provided to generate the output data matrix from the red, blue and green data matrixes can take various forms. According to claim 17, the algorithm employs the difference of the values of the data matrixes representing red and green colors divided by the sum of the corresponding values of the data matrixes representing red and green colors. According to claim 36, the algorithm employs the difference of the values of the data matrixes representing red and green colors divided by corresponding values of the data matrix representing blue color. According to claim 37, the algorithm employs the difference of the values of the data matrixes representing red and green colors divided by corresponding values of data matrixes representing the difference between red and blue colors. According to claim 38, the algorithm employs the difference of the values of the data matrixes representing red and blue colors divided by corresponding values of the data matrix representing green color. The claimed system, including the computing device using an algorithm based on a principle that eliminates the adverse effects

of multiple scattering and alterations in the illumination, is neither taught nor suggested by the cited prior art.

Interview

In the aforementioned interview, the undersigned emphasized the deficiencies in the teachings of Groner, U.S. Patent No. 5,983,120, in that Groner fails to disclose a system including (1) a polarizing filter adapted to collect backscattered light subjected to multiple scattering events in the tissue, (2) a photosensitive array capable of detecting the backscattered and polarized light and converting the detected light to a collected information of digital values, and (3) a computing device adapted to receive the collected information, adapted to separate the collected information into data matrixes representing red, blue and green colors, respectively, and adapted to employ an algorithm to the data matrixes to generate an output data matrix representing the red blood cell concentration of the microcirculation. The undersigned pointed out that Groner instead avoids collection of light subjected to multiple scattering (see, for example, column 7, line 58-column 8, line 2), and provides no teaching relating to provision of data matrixes representing red, blue and green colors, respectively, or an algorithm for generating an output data matrix from the red, blue and green data matrixes. The Examiner agreed.

The Examiner and the undersigned also discussed the MxN matrix taught by Zinser, U.S. Patent No. 5,620,000. The undersigned pointed out that the MxN matrices of Zinser et al are obtained by moving a laser beam along a line of a scanned object and measuring the intensity of the light reflected during the scanning at fixed time intervals so that a series of M-measured values is obtained along the scanned line, which represent the reflected light intensities at M-

individual points along this scanned line, and then successively repeating such scanning along the first line so that each of the M-points along the line is measured N times to form the MxN matrix of measured values (see column 5, lines 46-65). The undersigned pointed out, and the Examiner agreed, that Zinser provides no teaching of data matrixes representing red, blue and green colors, respectively, or an output data matrix provided by employing an algorithm to the red, blue and green data matrixes. The undersigned pointed out, and the Examiner agreed, that incorporation of a means to generate the Zinser MxN matrix in the device of Groner would not result in the system of claim 12.

Finally, the undersigned and the Examiner discussed the disclosure in Nilsson, U.S. Patent No. 5,361,769, of a visual presentation of an examined body part with the aid of a color monitor wherein each measurement point, i.e., each picture pixel, is given a specific color corresponding to the size range with which the superficial blood circulation in corresponding measurement points on the body part lie. The undersigned pointed out, and the Examiner agreed, that Nilsson describes a conventional use of a color monitor and provides no teaching of a computing device adapted to separate collected information into data matrixes representing red, blue and green colors, respectively, and adapted to then employ an algorithm to the data matrixes to generate an output data matrix.

The Examiner indicated that the rejections would be reconsidered upon the filing of a response.

Official Action Rejections

In the Official Action, claims 12, 14, 15 and 20-22 were rejected under 35 U.S.C. §103(a) as being unpatentable over Groner, U.S. Patent No. 5,983,120, alone or in view of Shih, U.S.

Patent No. 6,061,176, Godik, U.S. Patent No. 5,699,797, Nilsson, U.S. Patent No. 5,361,769, and Zinser, U.S. Patent No. 5,620,000. Claim 13 was rejected under 35 U.S.C. §103(a) as being unpatentable over these references in further view of Crutchfield, U.S. Patent Publication No. 2002/0091320. Claims 16-18 and 36-38 were rejected under 35 U.S.C. §103(a) as being unpatentable over these references in further view of Nakakuki, U.S. Patent Publication No. 2004/0208393, and claim 19 was rejected under 35 U.S.C. §103(a) as being unpatentable over these references in further view of Takahashi, U.S. Patent No. 4,366,529.

The Examiner asserted that Groner discloses a method and apparatus to perform in vivo analysis of blood vessels to determine blood parameters such as concentrations and blood cell counts, and the apparatus includes a monochromatic and/or polarized illuminating light source, detecting means for detecting reflected light that is reflected from the illuminated object, a first polarizer to polarize light from the light source, and a second polarizer placed in a reflected light path between an illuminated object and the detecting means with a plane of polarization 90° relative to that of the first polarizer. The Examiner asserted that Groner discloses that reflected light is captured by an image capturing means, which is coupled to a computer to carry out scene segmentation and correction for blood characteristic analysis (column 8, lines 55-68).

The Examiner alternatively relied on Shih as disclosing an analog-to-digital converter to convert detected light into digital values and directly displaying images of circulation on a monitor, on Zinser as teaching the use of a matrix MxN of measured values which are subject to Fourier transform, on Nilsson as delivering measurement values to a computer 7 to determine blood circulation, along with a color monitor to display microcirculation in specific colors, and on Godik as disclosing display microcirculation behaviors of physiological liquids marked with

the help of pseudo-colors which could be red, green, and blue. The Examiner asserted it would have been obvious to combine Groner with Shih, Zinser, Godik and Nilsson to use red, green and blue and to display microcirculation to increase visualization and to use a computer that separates data into matrices that are red, green and blue. Crutchfield was relied on as teaching administration of a vasoactive drug, Nakakuki was relied on as teaching image data corresponding to red, green and blue may be divided into a group of pixels in a matrix, and Takahashi was relied on as teaching the use of a bundle of optical fibers in a flexible pipe.

These rejections are traversed and reconsideration is respectfully requested. The system of claim 12 is nonobvious over and patentably distinguishable from the device of Groner, alone or in combination with the additionally cited references. More particularly, the apparatus of Groner utilizes reflected (white) light, and employs polarization filters and a photodetector array. However, as noted above and discussed with the Examiner, Groner provides no teaching or suggestion of a system including (1) a polarizing filter adapted to collect backscattered light subjected to multiple scattering events in the tissue, (2) a photosensitive array capable of detecting the backscattered and polarized light and converting the detected light to a collected information of digital values, and (3) a computing device as included in the system of claim 12, and, particularly, a computing device adapted to separate collected information into data matrixes representing red, blue and green colors, respectively, and adapted to employ an algorithm to the data matrixes to generate an output data matrix representing the red blood cell concentration of the microcirculation. Additionally, Groner provides no teaching, suggestion or recognition that such a system as claimed can reduce distortion from multiple scattering and from varying light intensity.

To the contrary, the Groner apparatus requires use of a clear representation of the object (e.g. blood vessels or individual blood cells embedded in a semitransparent tissue matrix) in such a way that no internal multiple scattering of the light is allowed. See, for example, the Groner claim 1 which recites image capturing means for capturing a reflected image reflected from the illuminated blood at a depth less than a multiple scattering length. This requirement of the Groner apparatus is also stated at column 7, beginning at line 58: "The tissue covering the image portion must be traversed by light without multiple scattering to obtain a reflected image"; and at column 7, beginning at line 65: "Second, the light that is collected from the subject must reach an image capturing means without substantial scattering, i.e. the reflected image must be captured from a depth that is less than the multiple scattering length." Accordingly, the Groner apparatus is only capable of investigating vascular networks close to the skin surface in transparent tissues, for example, the mucosa or in the transparent skin of newborn infants, and is dependent of the indicated clear view of the object under investigation.

In contrast to the Groner apparatus, the system of the present invention does not require a clear view of an object in tissue. Rather, because the computing device is adapted to separate collected information into data matrixes representing red, blue and green colors, respectively, and is adapted to employ an algorithm to the data matrixes to generate an output data matrix representing the red blood cell concentration of the microcirculation, the combined amount of diffusely backscattered light is analyzed to extract information about the average local red blood cell concentration modulating the pixels of the red, green and blue planes. This system is immune to the Groner disadvantages of multiple scattering of light blurring the individual objects before the diffusely backscattered light reaches the photo-detector array for further

analysis. To the contrary, the system of the present invention is not restricted to analyzing blood at a depth less than a multiple scattering length but rather operates via analysis of tissue at a multitude of scattering lengths. Groner provides no teaching or suggestion of a system which overcomes such a problem and particularly provides no teaching, suggestion or recognition of a system including a computing device adapted to separate collected information into data matrixes representing red, blue and green colors, respectively, and adapted to employ an algorithm to the data matrixes to generate an output data matrix representing the red blood cell concentration of the microcirculation as claimed.

The deficiencies of Groner are not resolved by the secondary references. Specifically, Shih was relied on as disclosing an analog-to-digital converter to convert detected light into digital values. However, Shih does not disclose a computing device adapted to separate collected digital values into data matrixes representing red, blue and green colors and adapted to employ an algorithm to create an output data matrix. Accordingly, Shih does not resolve the deficiencies of Groner.

Godik was relied on as disclosing a display of microcirculation behaviors of physiological liquids which is marked with the help of pseudo-colors. However, Applicants find no teaching by Godik of a computing device adapted to separate collected information into data matrixes representing red, blue and green colors, respectively, and to then employ an algorithm to the data matrixes to generate an output data matrix representing the red blood cell concentration of the microcirculation, and, importantly, Applicants find no motivation in Godik to modify any of the teachings of Groner to result in a system as recited in claim 12. Thus, the pseudo-color image of Godik does not provide any suggestion of a system for generating, inter

alia, data matrixes representing red, blue and green colors, respectively, and an output data matrix by employing an algorithm to the data matrixes. As noted in the present specification, the output data matrix which is generated by the computing device in the system of claim 12 may subsequently be presented as a pseudo-color or shaded image on a computer display (see page 9). However, Godik provides no teaching or suggestion of a system for obtaining a data output matrix as recited in claim 12 which may then be translated for pseudo-color representation. Thus, Godik fails to resolve the deficiencies of Groner et al.

Nilsson was relied upon as disclosing an apparatus that delivers measurement values to a computer to determine blood circulation and includes a color monitor to display microcirculation in specific colors. However, as noted above, Nilsson fails to teach a computing device adapted to separate collected information into data matrixes representing red, blue and green colors, respectively, and to employ an algorithm to the data matrixes to generate an output data matrix representing the red blood cell concentration of the microcirculation. Importantly, Applicants find no motivation in Nilsson to modify any of the teachings of Groner to result in a system as recited in claim 12. Thus, the display of Nilsson does not provide any suggestion of a system for generating, inter alia, data matrixes representing red, blue and green colors, respectively, and an output data matrix representing the red blood cell concentration of the microcirculation by employing an algorithm to the data matrixes. As noted in the present specification, the output data matrix which is generated by the computing device in the system of claim 12 may subsequently be presented on a computer display. However, Nilsson provides no teaching or suggestion of a system for obtaining a data output matrix as recited in claim 12. Thus, Nilsson fails to resolve the deficiencies of Groner.

Zinser et al was relied upon as teaching a computer that collects a matrix MxN of measured values and a second matrix MxN of measured values which are subject to FFT Fourier transform and that matrices can be displayed on the screen of the computer as an image. However, as noted above, the MxN matrices of Zinser are obtained by moving a laser beam along a line of a scanned object, and measuring the intensity of the light reflected during the scanning at M fixed time intervals and repeating the scanning N-times. However, Zinser provides no teaching of a device or method which generates, inter alia, data matrixes representing red, blue and green colors, respectively, and an output data matrix by employing an algorithm to the red, blue and green data matrixes. Thus, Zinser's data matrices are not relevant to the computing device in the system of claim 12 and Zinser fails to resolve the deficiencies of Groner.

Crutchfield was relied on as disclosing administration of vasoactive drug. However, Crutchfield does not resolve the deficiencies of Groner and, specifically, does not teach a system comprising, inter alia, a computing device adapted to separate collected information into data matrixes representing red, blue and green colors, respectively, and adapted to employ an algorithm to the separated matrixes to generate an output data matrix representing the red blood cell concentration of the microcirculation as required by claim 12. Further, Applicants find no apparent reason of record for one of ordinary skill in the art to use any of the Crutchfield teachings to modify Groner.

Nakakuki was relied on as teaching that image data corresponding to red, green and blue may be divided into a group of pixels in a matrix and the luminance for each pixel may be represented as 8-bit data. However, Nakakuki discloses that for color image data, the image

data corresponding to red, green and blue may be divided into a group of pixels in a matrix, the luminance for each pixel is converted into a numerical value on a scale, and the relationship between a luminance and the number of pixels having that luminance is reviewed to control, for example, exposure timing for the image (see, for example, paragraphs [0031] and [0044]).

Nakakuki does not teach or suggest a computing device adapted to separate collected information into data matrixes representing red, blue and green colors, respectively, and adapted to employ an algorithm to the separated matrixes to generate an output data matrix representing the red blood cell concentration of the microcirculation. One of ordinary skill in the art would have had no apparent reason to combine the teachings of Nakakuki with Groner to provide such a device, as neither Nakakuki nor Groner teach or suggest the use of a computing device that employs an algorithm that coverts data matrixes representing red, blue and green colors into an output matrix representing a concentration of red blood cells with respect to variations in total light intensity from the illumination device and multiple scattering. Accordingly, the combination of Nakakuki and Groner cannot render obvious a computing device employing an algorithm that provides an output matrix from data matrixes of red, blue and green colors that represents red blood cell concentration in tissue without distortion and dependence of the illuminating light level. Thus, Nakakuki fails to resolve the deficiencies of Groner.

Finally, Takahashi discloses an illumination device for observing and photographing a portion of a body cavity to be examined with an endoscope and including a bundle of optical fibers. However, the Takahashi teachings are not directed to systems or methods for determining microcirculation and they provide no teaching or suggestion of a system for determining microcirculation based on a measured concentration of red blood cells. Importantly, Applicants

find no apparent reason of record for one of ordinary skill in the art to use any of the Takahashi teachings to modify Groner, particularly along the lines of the present system.

In determining patentability under 35 U.S.C. §103, it is necessary to determine whether there was an apparent reason to combine known elements in the fashion of the claims at issue, *KSR International Co. v. Teleflex, Inc.*, 550 US 398, 418 (2007). Applicants find no evidence of record which would provide any apparent reason to one of ordinary skill in the art to modify and supplement the teachings of Groner to result in a system as presently claimed which is operable to generate from data matrixes of red, blue and green colors an output data matrix representing the red blood cell concentration of the microcirculation and avoiding adverse effects of illumination and multiple scattering. Thus, the requisite showing that those of ordinary skill in the art would have had some apparent reason to modify the Groner system in a way that would result in the claimed system has not been made.

Accordingly, the system for determining microcirculation according to claim 12, and claims 13-22 and 36-38 dependent thereon, is nonobvious over and patentably distinguishable from the cited combinations of references based on Groner, and the rejections under 35 U.S.C. §103 have been overcome. Reconsideration is respectfully requested.

It is believed that the above represents a complete response to the Official Action and places the present application in condition for allowance. Reconsideration and an early allowance are requested. In the event that the application is not in condition for allowance, the Examiner is encouraged to call the undersigned to resolve any outstanding matters. Please charge any fee required with this response to Deposit Account No. 503915.

Respectfully submitted,

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